REMARKS

An Office communication mailed May 22, 2005 required restriction to six groups of claims, a further restriction to a sequence and for some groups, a species election. In response, Applicants provide amendments and the following remarks.

Applicants hereby elect Group II (claims 1, 2, 4-10, 25 and 26), drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor using ONE predictive marker wherein the level of expression of the marker is determined by detection of mRNA wherein the proteasome inhibition-based regimen for treating the tumor comprises treatment with bortezomib, classified in class 435, subclass 6, with traverse. To be fully responsive, Applicants restrict the predictive marker to Number 149, and elect the species of multiple myeloma. Applicants hereby reserve the right to further traverse the above restriction with respect to non-elected Groups I, and III-VI in this or subsequent applications.

Applicants herein cancel claims 3, 6, 8, 9, 11-24 and 27-28. Applicants are amending claims 1, 2, 4, 25, and 26 and are adding new claims 29-41. Upon entry of the amendments, claims 1, 2, 4, 5, 7, 10, 25, 26 and 29-41 will be pending. No new matter is being added.

Support for the amendments to claim 1 can be found in the specification at, for example, paragraphs [0018], [0056], [0050], [0061] and [00220]. Support for the amendments to claim 4 can be found in the specification at, for example, paragraph [00229]. Support for the amendments to claim 25 can be found in the specification at, for example, paragraph [0025]. Support for new claims 29 and 30 can be found in the specification at, for example, paragraph [00222]. Support for new claims 31 and 32 can be found in the specification at, for example, paragraphs [0011] and [0012], respectively. Support for new claim 33 can be found in the specification at, for example, paragraph [0082].

The Restriction Requirement mailed May 22, 2005 is being traversed for the following reasons:

The Examiner has divided the 28 claims of the present application into 6 main groups, and further divided the claims according to a single marker per group. (This ignores the fact that claims 21 and 22, of Group I recites "at least two" for a marker set.) The Examiner appears to be

preparing to search the invention in terms of pure molecular sequences. The consequence of this is that the effective number of groups will number in the thousands, which ignores many of the teachings of the Applicants.

Applicants submit that there is an alternative position from which to view the claims. Applicants request that the Examiner consider that the Restriction be viewed in terms of treatment method in general, rather than getting mired in the details of the individual markers. For some time, the prediction of disease by marker analysis has been moving away from analysis of single markers and toward the analysis of multiple markers. This genetic profiling has become scientifically and commercially accepted (see, e.g., Van de Vijver et al. and Barden et al., provided in the IDS). The markers provided in Tables 1, 2 and 3 can be viewed as starting material for predictive marker sets associated with responsiveness, non-responsiveness, time-to-progression, or refractory nature of tumors for which bortezomib treatment is contemplated. Tables 4-8 represent studies wherein various statistical or scientific methods were applied to provide non-limiting examples where the principles of generating predictive marker sets were applied or validated.

To illustrate this line of reasoning, Applicants herein amend claims 1, 2, 4, and 25 to claim a method to determine bortezomib treatment of a liquid tumor starting from the markers in Table 1. In this illustration, only "bortezomib" needs to be searched in relation to a liquid tumor and genetic profiling or predictive marker sets. Then, the overall content of Table 1 (e.g., total number of genes, whether the profile or marker set predicts responsiveness, non-responsiveness, time-to-progression, or refractory nature of tumors, the names of probesets or representative genes, relative rank of markers, etc) can be perused in any resultant profiles or sets identified in the search.

In a way, even if the Examiner does not agree with this proposal, claims 1, 2, 4, 5, 7, 10, 25, 26 and 29-33 can be considered to fit alongside Group II, somewhat as generic claims for the elected group or marker No. 149. For example embodiments of these claims recite Table 1, where elected marker No. 149 is found; they have been limited to nucleic acid sequences, etc..

Agent for Applicants will be happy to discuss this reasoning and proposal if the Examiner is unclear or has any suggestions.

This paper is being filed timely as a request for a four month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

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